SEMA Lab Crowdfunding Overview
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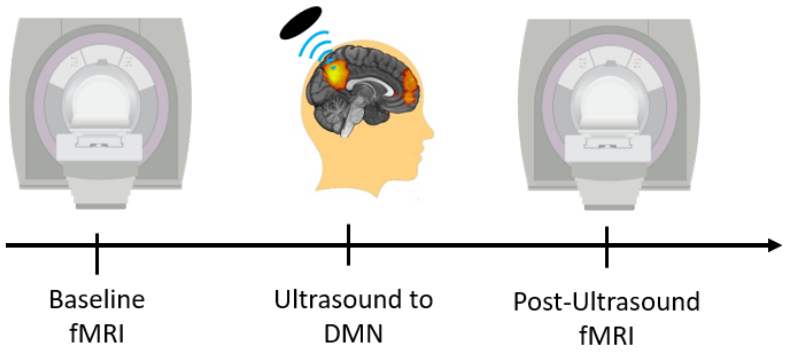
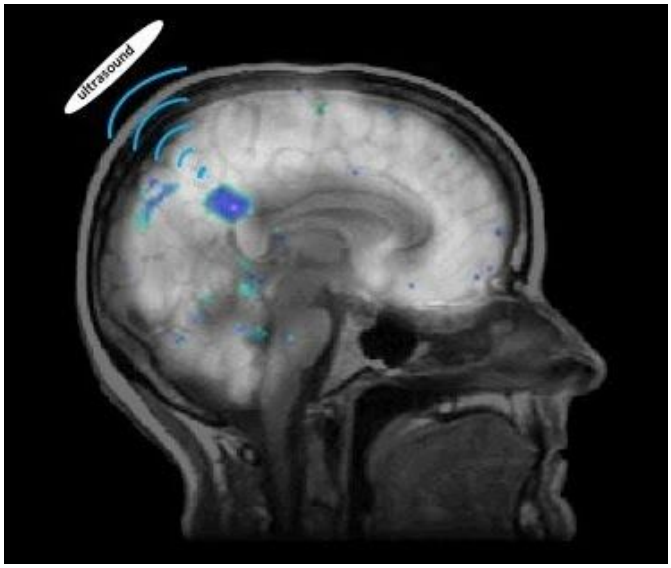
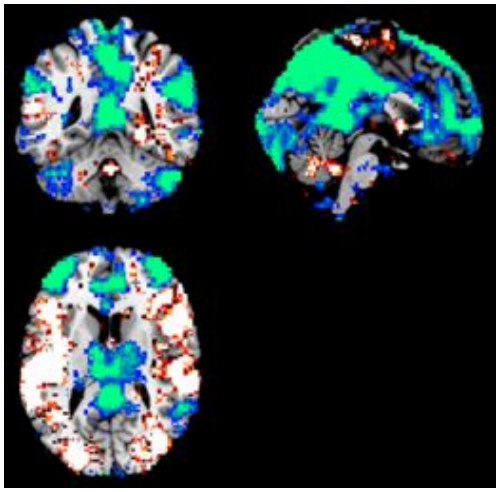
Pilot results (unpublished; manuscript in preparation)



Experimental timeline. Participants (N=6) had baseline resting-state fMRI recorded (3T Siemens Skyra scanner). Subjects were healthy with no prior history of mental disease and no experience with mindfulness or meditation. They had 10 minutes of transcranial focused ultrasound targeting the posterior cingulate cortex (130 total ultrasound stimulations, 500 kHz, ~500 mW/cm^2 ISPTA), a major hub of the default mode network outside of the scanner. They were put back in the scanner and received a post-ultrasound resting-state fMRI scan.



Neuroimaging results: Pre-post brain scans revealed a significant decrease in brain activation in the posterior cingulate cortex. Blue in the brain images above indicates reduction in brain activity relative to baseline. Only significant results are shown, $p < 0.05$, FDR corrected.

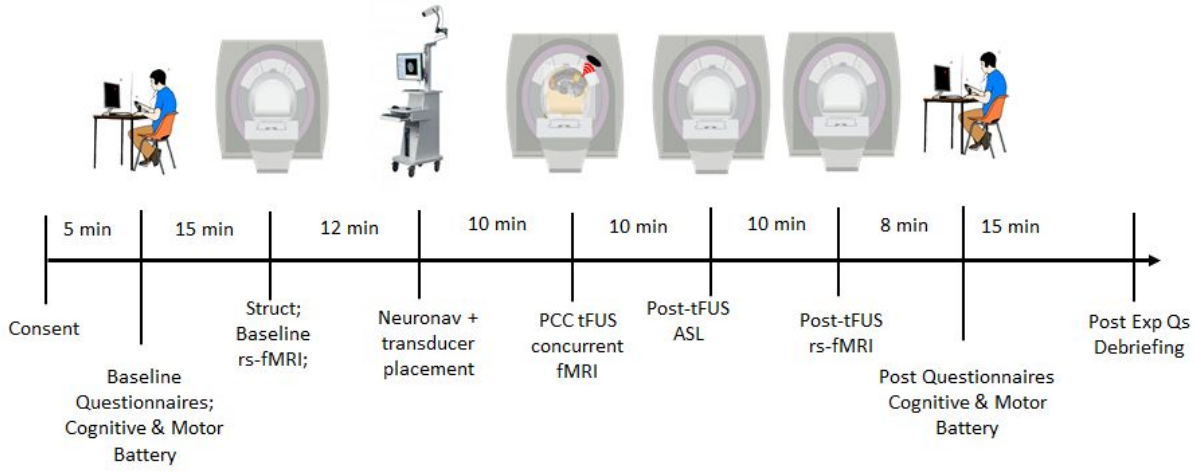


Resting-state functional connectivity results: The posterior cingulate cortex (PCC) was seeded. Blue indicates significant decreases in functional connectivity with the PCC. In the bottom left image, you can see decreases within the DMN along the midline structures in the brain, and decreased connectivity with areas in the right and left prefrontal cortex (FDR corrected).

Experiment 1

fMRI Combined with Transcranial Ultrasound to Enhance Mindfulness
Total budget: $20,226

Experimental design overview



Experiment Goal

To demonstrate that transcranial ultrasound targeting the posterior cingulate cortex - a major hub of the Default Mode Network - enhances a core component of mindful awareness called equanimity and task-dependent behavior.

Full Abstract

Introduction: Mindfulness is a form of awareness that brings attention to the present moment on purpose. Mindful awareness is composed of three core skills, concentration, sensory clarity, and equanimity, that can be developed with practice. The development of mindful awareness is linked to positive health outcomes and the reduction of clinical symptoms like chronic pain and addiction. However, mindfulness training initially takes time and effort, which presents many patients from experiencing the benefits. The posterior cingulate cortex (PCC), a major hub of the Default Mode Network (DMN), is proposed as a target of mindfulness practice. In a pilot experiment, we found that temporarily inhibiting the PCC with ultrasound neuromodulation reduced PCC activity, DMN connectivity, and increased self-reported equanimity. Here, we seek to replicate our pilot experiment with a double-blind, placebo controlled experiment with cognitive tasks to monitor for changes in behavior.

Methods: Baseline self-report mindfulness scales (Toronto Mindfulness Scale; Five Facet Mindfulness Questionnaire; Equanimity Scale), and cognitive and motor tasks (Self-reference task; Emotional Posner Cueing; Choice Reaction Time) will be administered. Resting state fMRI will be recorded (N = 20) at baseline. Transcranial focused ultrasound (tFUS; 500 kHz, PD = 36 μs, PRF = 100, Ispta = ~500 mW/cm2) will be delivered to the posterior cingulate cortex for 10 minutes (130 total ultrasound stimuli) while fMRI is concurrent record. Self-report scales and the tasks listed above will be given again for a post-sonication assessment.

Hypothesis: No changes are predicted in the placebo-control group for neuroimaging (fMRI), task effects, or self-report scales. The active tFUS group will be tested against the placebo-control group. The prediction is that inhibitory tFUS to the PCC will decrease PCC BOLD activation and DMN functional connectivity whereas. PCC deactivation and DMN connectivity changes should increase reaction time on the Self-reference task, enhance disengagement time on the Emotional Posner Cueing task, and should not affect behavior on the Choice-Reaction Time task. Importantly, a reduction in PCC/DMN activity should be correlated with increased self-report measures of equanimity on the standardized mindfulness scales.

Discussion: Altered fMRI BOLD activation in the PCC, coupled with decreased functional connectivity in the DMN, would suggest that tFUS temporarily reduced activity in a brain region linked to mindfulness practice. Increased self-report equanimity would provide converging evidence that the PCC is related to states of equanimity. Decreased disengagement time on the Emotional Posner Cueing task would suggest that participants were less reactive (ie, more equanimous) to emotional interference cues. On the other hand, increased reaction times on the

self-reference task might highlight decreased self-referential processing due to altered DMN connectivity. Finally, no change on the Choice-Reaction Time task would support the safety of this intervention as the PCC/DMN may be crucially involved in cognitive control (specifically regulating the balance between internally and externally directed cognition). Collectively, these results would suggest that tFUS targeting the PCC could modulate network level activity related to equanimity, a cornerstone of mindful awareness, and enhance behavior related to equanimity (disengagement). Future experiments investigating whether combining mindfulness training with PCC tFUS may facilitate learning equanimity and mindful awareness in general are warranted.